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Appropriate hemoglobin A1c testing frequency to monitor patients with type 2 diabetes



ABSTRACT

Background: Glycated hemoglobin (HbA1c) is used to monitor glycemic control among patients with type 2 diabetes (T2DM). HbA1c represents a 3-month glycemic average, with the most recent 6 weeks of glycemia having greatest influence. Analytical and biological variation introduce imprecision into any single HbA1c, where a result of 7.5% may represent a “true” value between 6.8% and 8.2%.

Aims: This *Therapeutics Letter* evaluates the most appropriate interval for monitoring HbA1c in T2DM.

Methods: Evidence was synthesized from a pragmatic randomized controlled trial (RCT) and three large observational studies.

Results: In the RCT, 94% of patients monitored every 6 months maintained good glycemic control compared to 92% of those monitored every 3 months. Observational data indicated that 3-month testing resulted in a clinically unimportant difference in HbA1c compared with 6-month testing. Furthermore, patients tested 2 to 3

times annually were as likely to achieve personalized goals as those tested 4 times per year. Testing more than 4 times annually was associated with a lower probability of achieving targets.

Conclusions: For patients with stable T2DM meeting glycemic goals, monitoring HbA1c every 6 months is as effective as every 3 months and could be contemplated for many patients following a discussion of patient goals and preferences. Frequent testing may be reserved for periods of medication adjustment, changes of health status, or when targets are unmet. Reducing testing frequency in stable patients minimizes low-value data, reduces the carbon footprint of lab testing, and improves patient convenience without compromising clinical outcomes.

Keywords: Blood Glucose; Diabetes Mellitus; Glycated Hemoglobin; Physiologic Monitoring.



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Vignette: Your 68-year-old patient with type 2 diabetes has taken metformin 1000mg twice daily, and empagliflozin 10mg once daily for the last 6 years. Over this interval, you checked his HbA1c (A1c) every 3 months – 24 times, so far. It has ranged from 6.7% to 7.4% for the last two years. **Should you continue to re-test the A1c every 3 months?**

Summary and Conclusions

- **The optimal A1c monitoring interval to improve clinical outcomes for people with type 2 diabetes has not been established from controlled clinical studies.**
- **Observational studies suggest that monitoring A1c every 3 months is not better than less frequent monitoring (e.g., every 6 months) to achieve glycemic targets.**
- **Be cautious about over-interpreting any single A1c result, or a small change in A1c, because of imprecision around any A1c result.**
- **As with other tests, ordering an A1c makes sense only if a result is likely to lead to a change in care.**

HbA1c biochemistry and physiology

Glucose attaches to hemoglobin inside red blood cells (RBC), creating glycated (sugar-coated) hemoglobin.¹ The proportion of hemoglobin that is glycated is closely correlated with the average concentration of glucose in the bloodstream over time and is reported as A1c.^{1,2} A1c does not require fasting or a timed sample.

Because red blood cells live about 120 days (range 70 to 140 days)^{3,4} an A1c test provides an estimate of a person's average blood glucose level over the previous 3 months.² However, blood glucose levels in the 6 weeks immediately before an A1c test have greater influence on the result than levels in the first half of a 3-month interval.⁵

Any condition that increases the lifespan of a RBC or reduces RBC turnover can result in misleadingly elevated A1c results – for example, untreated iron deficiency and other nutritional deficiency anemias which slow erythropoiesis.⁵ Conversely, conditions that shorten RBC lifespan, such as acute or chronic bleeding and advanced kidney disease, may result in misleadingly low A1c results.⁵



More important for patient care is typical biological (physiologic) and analytical (laboratory) variability that affects the interpretation of patient monitoring.⁶ For any single measurement of A1c, the imprecision (from both biological and analytic variability) of a result may be such that an A1c of 7.5% could reflect a “true A1c” somewhere between 6.8% and 8.2%.⁶ For this reason, it is a mistake to weigh heavily any single A1c value, or a small change in A1c over time. Rather, it is important to consider the trend of A1c values along with the imprecision that exists around a single value.

How often should we check A1c to monitor people with type 2 diabetes?

Because it takes time for A1c to reflect any change in glucose levels, it does not usually make sense to check A1c within 3 months of a previous test.

Several studies have examined the impact of different A1c monitoring intervals on achieving A1c goals in people with type 2 diabetes (T2DM), although not on clinical outcomes. The only randomized controlled trial (RCT) on this topic was a pragmatic trial conducted in people with T2DM and an A1c <7.5% (N=2,215) and followed for 18 months.⁷ This evaluated glycemic control from testing A1c every 3 months versus 6 months. In the “every 3 months” group, 92% remained in good control, versus 94% in the “every 6 months” group. The investigators concluded that there was no clinically relevant difference between every 3 months versus every 6 months A1c testing.

In 2 non-randomized observational studies (N=79,409 and N=19,908), testing A1c every 3 months (q3/12) versus every 6 months (q6/12) was associated with a very small decrease in A1c: about 3% relative reduction over 2-4 years.^{8,9} This would correspond to a change in mean A1c from 7% to about 6.8% – an accomplishment of no clinical relevance.

Finally, a large cohort study (N=20,690) followed people with T2DM for up to 4 years. Even in those whose A1c was considered “sub-optimal”, testing every 6 months achieved A1c goals as well as testing every 3 months.¹⁰ Undergoing only a single annual test or >4 tests per year were



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both associated with a lower probability of achieving a target A1c. **People having 2-3 A1c tests annually were as likely to achieve a personalized goal as those who underwent 4 tests per year.** Thus, available evidence casts doubt on any clinical advantage of testing every 3 month versus less frequently.

No study has assessed how the frequency of A1c testing influences clinical outcomes that are important to people with T2DM.

For monitoring of T2DM, Canadian and British Columbia Guidelines make the following suggestions:^{2,11}

- Check A1c every 3 months when blood glucose targets are not met, or when changes in diabetes management are underway.
- Check A1c every 6 months when blood glucose goals are met, and management is stable.

The available evidence reviewed above provides additional nuance to these recommendations and supports the notion that less frequent testing (e.g., every 6 months) could be considered for many patients after a discussion of patient preferences and goals. Reducing unnecessary or low value tests is suggested to have the highest potential to reduce the carbon footprint of pathology testing.¹² For patients, this means less travel and inconvenience, as well as fewer venipunctures. For clinicians, it may also mean fewer data to handle in a busy day.¹³

These considerations do not apply to patients with unstable trajectories caused by changes in health status or concomitant treatments, or situations where treatment is being adjusted to respond to severe hyperglycemia. In these situations, more frequent A1c testing may be appropriate.

What is the purpose of A1c monitoring?

The utility of A1c monitoring is to achieve glycemia in a range that meets clinician and patient goals for diabetes care. Glycemic goals should be individualized. For most people with T2DM, it is reasonable to target moderate A1c goals from 7% to 8%,¹⁴ considered as the average of several measurements – rather than any single test. More relaxed goals may be appropriate in frail, older adults, whereas more stringent goals (e.g., A1c <7%) might be reasonable in people with recent onset T2DM, low risk of adverse effects from treatment, low treatment burden and longer life expectancy.¹⁴⁻¹⁷

In T2DM the importance of achieving A1c targets <7% has been challenged¹⁸ despite guideline recommendations.^{17,19} This is because targeting A1c at <7% versus <8% does not reduce the incidence of premature death or cardiovascular events, but it does increase hypoglycemia risk.¹⁴ Recent large RCTs of the sodium glucose cotransporter-2 inhibitors (SGLT2i) and glucagon-like peptide-1 receptor agonists (GLP-1RA) achieved improvement in outcomes meaningful to patients – such as major adverse cardiovascular events – with mean achieved A1c in the mid 7% range.²⁰⁻²²

Achieving an A1c <7% has been shown to reduce microvascular outcomes, although these improvements are primarily in surrogate markers such as albuminuria rather than clinically important outcomes such as vision loss or dialysis.^{14,18} Achieving a strict low target A1c can require complex and burdensome treatment regimens. Thus, individualized care should balance possible benefits with the burden of medications and adverse effects.

Vignette resolution: *Your patient's pharmacological regimen is stable, and his A1c reflects glycemic control within a range clinically appropriate at age 68. When you suggest reducing the frequency of A1c tests to every 6 months, he is relieved to undergo fewer blood draws and reduce his trips to the laboratory. This inspires you to consider other patients who could benefit similarly, and reassess the frequency with which you requisition A1c and other common laboratory tests.*

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Understanding your A1c test: do you need it every 3 months?



PLAIN LANGUAGE SUMMARY

What is an A1c test?

An A1c test measures your average blood sugar over 3 months. The results show how your medicine is working and whether changes are needed.

Why do I usually get tested every 3 months?

Doctors often check A1c every 3 months. However, if your blood sugar has been in your target range for a year or more and your treatment hasn't changed, testing every 3 months might not be necessary.

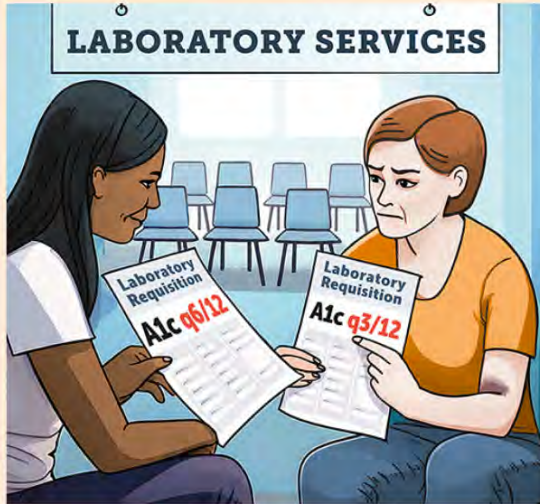
Is testing every 3 months better than every 6 months?

Research shows that for patients with stable type 2 diabetes, testing every 6 months is just as good as testing every 3 months. In a large study of over 20,000 people, those tested twice a year stayed in control just as well as those tested four times a year. Testing more often did not lead to better health.

When should I talk to my doctor about testing A1c less often?

If your A1c has been stable for a year or more, and you aren't changing your medications, you can ask about being tested every 6 months instead of every 3 months. This means:

- Fewer trips to the lab and fewer needle pokes.
- Less travel and more saved time for you.
- Lower costs for the healthcare system.



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How often should I have an A1c test?

What is an A1c test?

- An A1c test measures your average blood sugar over three months.
- The results show how your treatment is working or whether changes are needed.

A test every 3 months?

If your blood sugar has been steady and in your target range for a year or more, you might not need to be tested every three months.

Is it safe for me to be tested less often?

Research shows that patients with stable Type 2 diabetes do just as well with testing every six months instead of every three months.



Talk to your doctor



- Discuss whether testing less often makes sense for you.
- This will mean fewer lab trips.

Learn more: <https://ti.ubc.ca/letter161>

